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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/976,566	11/24/1997	ANDREW A. POTTER	9001-0016.01	2057

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EXAMINER	
GRASER, JENNIFER E	
ART UNIT	PAPER NUMBER
1645	27

DATE MAILED: 02/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/976,566	Applicant(s) Potter et al.
	Examiner Jennifer Graser	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Request for CPA, 1/22/02*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *37, 40, 41, 44, and 45* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *37, 40, 41, 44, and 45* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 1/22/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/976,566 is acceptable and a CPA has been established. No new amendments have been received. An action on the CPA follows.

Double Patenting rejections

2. A Terminal Disclaimer was received with the After Final Amendment filed January 12, 2000. Accordingly, the former Double Patenting rejections have been dropped.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a

later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

4. Claims 37, 40, 41 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over as being unpatentable over Potter (5,476,657) in view of Bell et al (5,114,711).

Potter discloses proteins and subunit antigens from *P.haemolytica* for use in stimulating immunity against respiratory diseases such as pneumonia, including shipping fever pneumoniae (see abstract). Vaccines comprising an immunogenic amino acid sequence of *P.haemolytica* leukotoxin, or an amino acid sequence substantially homologous and functionally equivalent thereto, and a pharmaceutically acceptable carrier are disclosed (column 3, lines 3-24). Potter discloses production of recombinant *P.haemolytica* leukotoxin and specifically recites the production of leukotoxin 352 or "LKT 352" (column 17, lines 54-58). It is disclosed that vaccination with LKT 352 in combination with a *P.haemolytica* saline extract significantly reduced bovine respiratory disease morbidity and bovine respiratory disease mortality as compared to treatment with a placebo (column 25, lines 43-48). It is also specifically disclosed that prior to immunization, it may be desirable to increase the immunogenicity of the particular Pasteurella protein, or an analog of the protein, by linking the antigenic peptide to a carrier (column 13, lines 10-15). It is disclosed that suitable carriers may be proteins, polysaccharides, VP6 polypeptides of rotaviruses, viral proteins (column 13, lines 9-50). However, Potter does not particularly exemplify chimeric proteins comprising a leukotoxin derived from *P.haemolytica* and a peptide hormone, such as gonadotropin releasing hormone (GnRH) or an epitope thereof.

Bell et al. disclose the recombinant production of chimeric proteins which are composed of two covalently linked cell modulators in a linear polypeptide sequence. It is taught that the cell modulators are interferons, lymphokines or cytokines (abstract). Column 3, lines 60-64, define cell modulators as including lymphokines, monokines, peptide hormones, or peptide growth factors.

At the time the invention was made it was well known in the art to those of ordinary skill that many different protein combinations could be prepared recombinantly that produce chimeric proteins and it was also well established that various immune modulators have been conjugated to such things as antibodies, ligands, or hormones, to act as site-specific delivery agents (some of which also display functional activity of the cytotoxin). Potter specifically discloses that the immunogenicity of the *P.haemolytica* leukotoxin (a cytotoxin), and fragments thereof, could be made more immunogenic by linking it to a carrier such as proteins, polysaccharides, inactive virus particles and other large, slowly metabolized molecules (column 13). Bell et al. specifically disclose that cytotoxins and peptide hormones may be linked together to treat disease. It would have been obvious to one of ordinary skill in the art at the time the invention was made that a peptide hormone as disclosed by Bell et al. could be linked to at least one epitope of a leukotoxin derived from *P.haemolytica,* as taught by Potter, because the leukotoxin is a cytotoxin which Bell specifically teaches may be linked to peptide hormones, for a dual immune modulating effect. One of ordinary skill in the art would expect to increase the immune response to the leukotoxin and produce a more efficient vaccine against respiratory disease in

ruminants by linking to an immune modulator. Potter specifically discloses that truncated leukotoxin, LKT 352, which lacks cytotoxic activity could be used as the *P.haemolytica* leukotoxin. Bell discloses the use of adjuvants and carriers and it would have been obvious to one of ordinary skill in the art to link the cytotoxin-peptide hormone to a carrier as the use of linking carriers to chimeric proteins was well known in the art for a means of increasing an immune response to an antigen. Although the use of gonadotropin releasing hormone is not specifically recited by Bell et al., it would have been an obvious choice in the cytotoxin-immunomodulator conjugates because it is a well known hormone which falls under the definition of "peptide hormone". These compositions would be structurally identical to those instantly claimed, i.e., a chimeric protein comprising leukotoxin coupled to a peptide hormone which is not a cytokine.

Response to Applicants' arguments:

Applicants have argued that the amendment to claim 37 which states that the leukotoxin polypeptide is coupled to a "selected peptide hormone which is not a cytokine" is sufficient to overcome the rejection. This argument has been fully and carefully considered but is not deemed persuasive because Bell et al discloses the use of immune-modulators other than cytokines in the cytotoxin conjugates. Column 3, lines 60-64, of Bell defines cell modulators as including lymphokines, monokines, peptide hormones, or peptide growth factors.

5. This is a CPA of applicant's earlier Application No. 08/976,566. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the

grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

2/4/02

Jennifer Graser
Primary Examiner
Art Unit 1645